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TABLE 2

Stability data of compound 1/medium chain fatty acid triglyceride (MCT) solution (60 µg/g)		
gelatin piece		concentration
plasticizer	water content (after dried)	of compound 1 after storage ¹⁾
glycerin	23%	86.8%
sugar alcohol solution derived from corn starch ²⁾	25%	92.0%

¹⁾Percentage based on a theoretical amount (60 µg/g)²⁾Polysorb 85/70/00™, ROQUETTE AMERICA, Inc.

According to the reference example 1, in case the 15-keto-prostaglandin compound of the invention and the sugar alcohol were contacted directly, stability of the compound was significantly lowered. In contrast, in case the 15-keto-PG compound was directly contacted with a polyol such as glycerin, the stability of the compound was maintained. It has surprisingly revealed by Example 1 that the stability of the 15-keto-prostaglandin contacted with gelatin piece prepared using sugar alcohol as a plasticizer was better than that contacted with gelatin piece with glycerin as a plasticizer.

Example 2

Sugar alcohol solution derived from corn starch in an amount shown in Table 3 was added in an appropriate amount of water, stirred and heated. Then, gelatin 100 parts by weight was added thereto to give gelatin solution. Compound 1 was dissolved in medium chain fatty acid triglyceride (USP/NF grade) to give a fill solution containing 240 µg/g of compound 1. The gelatin solution and the liquid mixture were loaded on capsule forming and filling machine to give capsule containing the fill solution therein, and the capsule was dried to give soft gelatin capsule.

The capsule was put in a sealed container and kept at 40° C. for 3 months. The concentration of compound 1 in the fill solution contained in the capsule was determined after 1, 2 and 3 months storage in the same manner as Reference Example 1.

TABLE 3

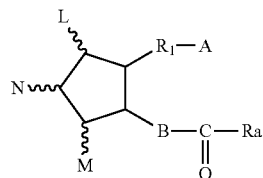
Stability of soft gelatin capsule of compound 1						
soft gelatin capsule				conc. (% of Initial) 40° C.		
(parts by weight)				1 mo	2 mo	3 mo
gelatin	100	sugar	35	99.9%	100.3%	99.2%
		alcohol	45	—	100.5%	100.0%
		solution ¹⁾	55	—	99.3%	100.0%

¹⁾Polysorb 85/70/00™, ROQUETTE AMERICA, Inc., derived from corn starch

The invention claimed is:

1. A soft gelatin capsule formulation of a 15-keto-prostaglandin compound, which comprises:
 - a soft gelatin capsule shell comprising gelatin and sugar alcohol as a sole plasticizer, and
 - a mixture comprising a 15-keto-prostaglandin compound and a pharmaceutically acceptable vehicle, which is filled in the shell.
2. The formulation of claim 1, wherein the 15-keto-prostaglandin compound is a compound of the formula (I):

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wherein L, M and N are hydrogen, hydroxy, halogen, lower alkyl, hydroxy(lower)alkyl, lower alkanoyloxy or oxo, wherein at least one of L and M is a group other than hydrogen, and the five-membered ring may have at least one double bond;

A is —CH₃, or —CH₂OH, —COCH₂OH, —COOH or a functional derivative thereof;

B is —CH₂—CH₂—, —CH=CH— or —C≡C—;

R₁ is a saturated or unsaturated bivalent lower or medium aliphatic hydrocarbon residue, which is unsubstituted or substituted with halogen, lower alkyl, hydroxy, oxo, aryl or heterocyclic group, and at least one of carbon atom in the aliphatic hydrocarbon is optionally substituted by oxygen, nitrogen or sulfur; and

Ra is a saturated or unsaturated lower or medium aliphatic hydrocarbon residue, which is unsubstituted or substituted with halogen, oxo, hydroxy, lower alkyl, lower alkoxy, lower alkanoyloxy, cyclo(lower)alkyl, cyclo(lower)alkyloxy, aryl, aryloxy, heterocyclic group or heterocycloxy group; lower alkoxy; lower alkanoyloxy; cyclo(lower)alkyl; cyclo(lower)alkyloxy; aryl; aryloxy; heterocyclic group; heterocycloxy group.

3. The formulation of claim 1, wherein the 15-keto-prostaglandin compound is a 13,14-dihydro-15-keto-prostaglandin compound.

4. The formulation of claim 1, wherein the 15-keto-prostaglandin compound is a 15-keto-16-mono or 16,16-di-halogen-prostaglandin compound.

5. The formulation of claim 1, wherein the 15-keto-prostaglandin compound is a 13,14-dihydro-15-keto-16-mono- or 16,16-di-halogen-prostaglandin compound.

6. The formulation of claim 1, wherein the 15-keto-prostaglandin compound is a 15-keto-16-mono- or 16,16-di-fluoro-prostaglandin compound.

7. The formulation of claim 1, wherein the 15-keto-prostaglandin compound is a 13,14-dihydro-15-keto-16-mono- or 16,16-di-fluoro-prostaglandin compound.

8. The formulation of claim 1, wherein the 15-keto-prostaglandin compound is a 15-keto-prostaglandin E compound.

9. The formulation of claim 1, wherein the 15-keto-prostaglandin compound is a 13,14-dihydro-15-keto-16,16-difluoro-prostaglandin E₁.

10. The formulation of claim 1, wherein the 15-keto-prostaglandin compound is a 13,14-dihydro-15-keto-16,16-difluoro-18S-methyl-prostaglandin E₁.

11. The formulation of claim 1, wherein the pharmaceutically acceptable vehicle is a fatty acid ester or a polyol.

12. The formulation of claim 1, wherein the fatty acid ester is a glyceride.

13. The formulation of claim 1, wherein the sugar alcohol is selected from the group consisting of sorbitol, maltitol, sugar alcohol solution derived from corn starch, hydrogenated maltose syrup and a mixture thereof.

14. The formulation of claim 1, wherein the sugar alcohol comprises sorbitol and sorbitan as its major component.

15. A method for stabilizing a 15-keto-prostaglandin compound, which comprises: dissolving, dispersing or mixing the